



# COMPARISON OF NEUTROPHIL/LYMPHOCYTE RATIO AND TROMBOCYTE/LYMPHOCYTE RATIO VALUES BETWEEN TONSILLECTOMY AND A CONTROL GROUP

## NÖTROFİL LENFOSİT ORANI VE TROMBOSİT LENFOSİT ORANININ TONSİLLEKTOMİ VE KONTROL GURUPLARINDA KARŞILAŞTIRILMASI

COMPARISON OF NEUTROPHIL / LYMPHOCYTE AND TROMBOCYTE / LYMPHOCYTE RATIO VALUES ON TONSILLECTOMY

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### Öz

**Amaç:** Tonsillektomi yapılan hastalarda nötrofil lenfosit oranı (NLO) ve trombosit lenfosit oranının (TLO) tonsillektomi endikasyonu ile ilişkisini incelemek. **Gereç ve Yöntem:** 2012-2016 yılları arasında kronik tonsillit nedeniyle tonsillektomi yapılan 200 erkek çocuk çalışma grubuna alındı. Hastaların kayıtlarından anamnezleri kontrol edilip primer şikayeti sık tonsillit geçirme öyküsü olanlar seçildi. Aynı dönemde Üroloji ve Çocuk Cerrahisi kliniklerinde sünnet yapılmış 100 sağlıklı birey kontrol grubuna alındı. Hastaların dosyaları retrospektif olarak tarandı. **Bulgular:** Çalışmamızın sonucunda, çalışma grubu ve kontrol grubu arasında yaş, lökosit sayısı, nötrofil sayısı, trombosit sayısı, RDW değerleri açısından anlamlı bir fark saptanmadı. Lenfosit sayıları çalışma grubunda kontrol grubuna kıyasla daha düşük bulundu. Çalışma grubunda NLO ve TLO kontrol grubuna oranla yüksek bulundu. Bu yükseklik istatistiksel olarak anlamlı bulundu. (NLO ve TLO sırasıyla P=0.001, P=0.011, P<0.05) **Tartışma:** Sonuç olarak tonsillektomi yapılan hastalarda NLO'nun kontrol grubuna göre yüksek olduğunu tespit ettik. Onkolojik hastalarda görülen nötrofil artışına sekonder NLO yüksekliğinin tersine çalışmamızda lenfosit değerlerindeki düşmenin NLO artışına yol açtığını gözlemledik. TLO değerlerinde tonsillektomi yapılan hastalarda kontrol grubuna göre yüksek olduğunu tespit ettik. Bunu duruma trombosit sayısındaki artış değil, lenfosit sayısındaki azalmanın neden olduğunu gözlemledik. Çalışmamız tonsillektomi öncesi tespit ettiğimiz 1.48 ve üzerindeki NLO değerinin bir endikasyon nedeni olarak kullanılabilecek ancak endikasyonu güçlendirebilecek bir parametre olduğunu düşündürmektedir.

### Anahtar Kelimeler

Nötrofil Lenfosit Oranı (NLO); Trombosit Lenfosit Oranı (TLO); Tonsillektomi

### Abstract

**Aim:** To assess the relationship between tonsillectomy indications and neutrophil/lymphocyte ratio (NLR) and trombocyte/lymphocyte ratio (TLR). **Material and Method:** In our retrospective study, conducted between 2012-2016, the study group consisted of 200 boys whose chief complaint was frequent tonsillitis and who therefore had a tonsillectomy due to chronic tonsillitis. The control group consisted of 100 healthy boys who had been circumcised in the Urology or Pediatric Surgery Departments. The files of patients and controls were retrospectively evaluated. **Results:** There was no statistically significant difference between the study group and the control group in terms of age, leukocyte, trombocyte, neutrophil count, or RDW value. In the study group, NLR and TLR (p=0.001 and p=0.011, respectively) were higher than in the control group and these findings are statistically significant. **Discussion:** NLO was higher in the study group than the control group. We also observed that it was the decrease in the lymphocyte count that caused the higher NLR, unlike the situation with oncologic patients whose higher NLR values are due to increased neutrophil counts. Also, TLO was higher in the study group than the control group, due not to higher trombocyte counts but instead to lower lymphocyte counts. In conclusion we believe that while an NLO ratio of 1.48 can not serve as a definitive indication for tonsillectomy, it can be used to support already-established indications.

### Keywords

Neutrophil / Lymphocyte Ratio (NLR); Trombocyte / Lymphocyte Ratio (TLR); Tonsillectomy

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## Introduction

The ratios of neutrophils and lymphocytes, which are the elements of white blood cells, to the total count are parameters known and used for a very long time in medicine, particularly in the detection of infections and inflammation. Besides these well-established parameters, neutrophil/lymphocyte ratio and thrombocyte/lymphocyte ratio have recently come into focus as possible predictive or prognostic factors in some infections and malignancies. The frequency of studies on NLO and TLO has been increasing in recent years. A PubMed search revealed 339 papers written on NLO [1-4].

NLO and TLO have been designated as inflammatory markers that can be routinely studied in the peripheral blood without additional cost. The physiological response of leukocytes to stress includes increased neutrophil count, i.e. neutrophilia, with an accompanying decreased lymphocyte count, i.e. lymphopenia.

Because NLO and TLO are predictors of inflammation, the various fields in which they can be used are being highlighted in a number of new studies. For example, studies have been conducted not only on infections and cancers, but also peripheral facial paralysis, familial Mediterranean fever, vertigo, cholesteatoma, and adenoid vegetation [1-6].

Even so, in the literature there is only one study about NLO and TLO performed with patients who underwent tonsillectomy—a study conducted in 2015 in Turkey. In the present study, we assigned children who underwent tonsillectomy for tonsillitis in our clinic to the study group and children who underwent circumcision in the urology or pediatric surgery clinic to the control group. We then compared these two groups in terms of the values of NLO and TLO.

## Material and Method

A total of 200 boys aged 3-11 years, who had undergone tonsillectomy for chronic tonsillitis between 2012 and 2016 at Süleyman Demirel University School of Medicine, Department of Ear Nose and Throat (ENT), were assigned to the study group. We were careful to select cases who underwent tonsillectomy specifically for chronic tonsillitis. A total of 100 boys aged 2-12 years, who had undergone circumcisions in the same period in the Urology or Pediatric Surgery clinics, were assigned to the control group. Patients' medical records were retrospectively reviewed. The results of preoperative complete blood counts were evaluated by reviewing the patient files. Complete blood count was obtained by analyzing the blood samples, which were taken from the patients and the controls and placed into tubes containing calcium EDTA (Ethylenediaminetetraacetic acid) for use in an automated blood counter device (Beckman Coulter LH 780 Hematology Analyzer, USA). The blood count indicates absolute cell counts such as white blood cell count, leukocyte count, percentage distribution of white blood cells, neutrophil count, lymphocyte count, monocyte count, eosinophil count, basophil count, and platelet count. The value of NLO is obtained by dividing absolute neutrophil count by absolute lymphocyte count, and the value of TLO is obtained by dividing absolute thrombocyte count by absolute lymphocyte count. The values were compared between the study group that had undergone tonsillectomy and the healthy control group that had undergone circumcision.

Patients with any infectious disease, patients who underwent tonsillectomy for any reason other than chronic tonsillitis (asymmetric tonsil hypertrophy, mass, etc.), patients with chronic inflammatory disease, acute or chronic renal insufficiency, chronic liver disease, obstructive sleep apnea, connective tissue disease, inflammatory bowel disease and autoimmune disease, patients who had been receiving steroid therapy for any reason, who had asthma, who had been using drugs likely to increase serum neutrophil and leukocyte count, and those with malignant disease or immunosuppressive disease, were excluded from the study.

Statistical analysis of data was done using the SPSS 20.0 for Windows program. Statistical distribution was analyzed by two-sample Kolmogorov-Smirnov test. Student t-test was used for the variables with statistically good distribution, whereas non-parametric Mann-Whitney U test was used for the variables with statistically poor distribution. The study group and the control group were compared in terms of age, WBC, neutrophil count, lymphocyte count, RDW, NLO, thrombocyte, and TLO.

## Results

The comparison of the control group with the tonsillectomy group in terms of complete blood count is summarized in Table 1.

The two-sample Kolmogorov-Smirnov test revealed that the groups were not similar in terms of distribution of NLO ( $p<0.05$ ), and the Mann-Whitney U test demonstrated a statistically significant difference between the groups ( $p<0.05$ ). NLO was higher in the study group as compared to the control group. The Kolmogorov-Smirnov test revealed that distribution of TLO was not similar in the groups ( $p<0.05$ ) and Mann-Whitney U test demonstrated a statistically significant difference ( $p<0.05$ ). TLO was higher in the study group as compared to the control group. This supports the theory that NLO elevation was due to relative lymphopenia.

Tablo 1. Hasta grubunun ve kontrol grubunun tam kan sayımı değerlerine göre karşılaştırılması

	Tonsillektomi	Kontrol (sünnet)	p değeri
YAŞ	6.31 ± 1.86	5.78 ± 2.96	p=0.06
LÖKOSİT	8.31 ± 2.63	8.32 ± 2.14	p=0.957
NÖTROFİL	4.18 ± 2.13	3.50 ± 1.45	p=0.073*
LENFOSİT	3.25 ± 1.15	3.88 ± 1.43	p=0.000*
NLO (NLR)	1.48 ± 1.17	1.05 ± 0.79	p=0.001*
PLATELET	309.34 ± 88.90	328.20 ± 96.20	p=0.066
TLO(PLR)	102.77 ± 37.98	91.47 ± 31.35	p=0.011 *
RDW	14.23 ± 1.30	14.80 ± 2.26	p=0.071

NLO: nötrofil lenfosit oranı, TLO: trombosit lenfosit oranı, RDW: kırmızı küre dağılım genişliği. \*  $p<0.05$

## Discussion

Complete blood-leukocyte count is the most frequently used laboratory analysis. This test is an important, valuable, and practical screening method not only for hospital ENT departments but for all departments. Parameters of complete blood count are valuable for numerous disciplines in the presence of inflammation, infections, anemia, bleeding diathesis, and similar diseases, and they are mainly used for diagnosis. On the

other hand, these parameters are also used to evaluate efficacy of treatment and for patient monitoring. They are beneficial particularly in monitoring the course of infection and the efficacy of chemotherapy. While the ratios of neutrophil and lymphocyte counts to overall white blood cells count are well-established parameters, recent studies have also looked at the proportion (ratio) of white blood cell components to each other. Among these, NLO is the most frequently studied proportion. It is claimed that NLO might be a predictive or prognostic factor for some infections and malignancies.

A recent PubMed search using the key word "NLO" revealed 339 papers published in the year 2016. Searching for papers about ENT excluding malignancies, we found that elevated NLO has been investigated in facial paralysis, nasal polyp, cholesteatoma, and peritonsillar abscess [1-6]. The above-mentioned studies have compared NLO between nasal polyp patients and a healthy control group and determined high NLO in the nasal polyp patients; however, they found no difference in terms of TLO [2].

Similarly, Aktaş G et al. compared leukocyte and thrombocyte counts between nasal polyp patients and a healthy control group, but found no significant difference [2]. Ulu et al. evaluated NLO in patients with sudden hearing loss and found it higher as compared to the control group; they determined decreased response to treatment in the patients with high NLO and considered it as a prognostic factor [5]. Kılıçkaya et al. found NLO to be significantly higher in the patients with idiopathic facial paralysis. They determined a correlation between NLO and the degree of paralysis and stated that it may be a prognostic factor [1]. Kılıçkaya et al. determined no difference between the patients with and without cholesteatoma in terms of NLO [3]. In the study conducted by Yenigün, patients who underwent a surgical procedure for chronic tonsillitis were assigned to Group 1, whereas patients who underwent a surgical procedure for adenoid hypertrophy and tonsil adenoid hypertrophy were assigned to Group 2 and Group 3, respectively, and the control patients with anemia were assigned to Group 4 [7]. The difference in NLO in the adenoid hypertrophy and tonsil hypertrophy groups was found lower than that in the chronic tonsillitis group. Elevated NLO indicates the patient's inflammatory status. Yenigün found preoperative NLO to be higher than postoperative NLO in the chronic tonsillitis group ( $p=0.045$ ) [7]. The author defined the period from preoperative to postoperative time to be one month. However, we think it should not be expected for the patient's system to completely return to normal in such a short time, because complete improvement of inflammation in the surgical area sometimes takes more than one month following tonsillectomy. Moreover, the choice of control group is problematic; it is hard to know what the standard NLO is for children with anemia. In the present study, we did not perform postoperative evaluation because of expected difficulties of contacting the patients after surgery for control and blood sampling.

Yenigün defended the opinion that NLO might have a role in determining the timing of surgical intervention and in assessing postoperative local and systemic complications during postoperative follow-up in patients with chronic tonsillitis [7]. However, the author did not specify the NLO value at which the surgery

would be necessary for chronic tonsillitis, although it was noted that the value of NLO was  $1.98 \pm 1.01$  in the patients who underwent a surgical procedure for chronic tonsillitis. In the present study, we found NLO to be  $1.48 \pm 1.17$  in the patients that underwent tonsillectomy, whereas it was  $1.05 \pm 0.7$  in the control group. Yenigün reported NLO to be  $1.48 \pm 0.47$  in the control group [7]. In 2016, Derin et al. conducted a study that detected no significant difference between preoperative and postoperative values of NLO (1.0 and 1.06, respectively) in the patients who underwent adenoidectomy for obstructive sleep apnea [6]. Since NLO is a parameter that varies according to the individual, there is no absolute value for a given pathology. We think that the neutrophil/lymphocyte ratio used as an indication should be identified in each clinic instead of relying on an absolute value. NLO can be used as an auxiliary parameter to support the agreed indications of tonsillectomy. While the mean value of NLO was found to be 1.0 by Derin et al. [6], Yenigün et al. found the mean value of NLO to be 1.54 for postoperative tonsillectomy and 1.32 for postoperative adenotonsillectomy. In the present study, the values were 1.48 for the study group and 1.05 for the control group. The result of the control group was almost identical to that of the adenoidectomy group in the study conducted by Derin et al. In another study, Senturk et al. found both NLO and MPV to be higher in a peritonsillar abscess group than in a control group; they reported the cut-off value of NLO to be 3.08. This suggests a probable correlation between the severity of infection and NLO.

Yenigün et al. declared the limitations of their study as the absence of comparison of NLO with CRP and other inflammatory markers [7]. Because of the small sample size, the author found no correlation between NLO and the severity of chronic tonsillitis (e.g. incidence of tonsillitis, antibiotic use, quality of life). Moreover, no correlation was determined between postoperatively decreased NLO and decreased incidence of disease and suggested that NLO decreases while the disease is ongoing. The limitations of the present study include the absence of comparison between preoperative and postoperative values, inability due to inadequate recording to discriminate infection from obstruction while considering the indications of tonsillectomy, and the fact that the study and control groups consisted of male patients only.

In acute bacterial infection, the circulating neutrophil count increases within hours or even within minutes, because neutrophils are present in the stores as marginated and pass into the circulation when required. However, unlike neutrophils, lymphocytes are not present in the stores; they are produced when needed and pass into the circulation. For this reason, since mainly the neutrophils are responsible for immunity in acute bacterial infections, they accumulate rapidly in the relevant area, leukocytosis is completed, and lymphocytes are reduced in this period. NLO elevation is expected in acute infection since the neutrophil count is quite high. When the infection decreases, neutrophils are sequestered again and neutrophil count returns to the normal. In the present study, NLO was found to be normal in this case, i.e., when there was no question of infection and the leukocyte count was normal. Statistical analysis of data indicated decreased lymphocyte count as the reason for elevated NLO in the study group. There was no statistical

difference between the study group and the control group in terms of neutrophil count; however, lymphocyte count was significantly lower in the study group. In our opinion, since chronic infections present themselves with acute exacerbations, neutrophils are found as margined and are normal in count at the point in recovery when there is no infection, but lymphocytes are low in the post-infection period. Therefore, NLO is found to be high in uninfected patients during preoperative examination for tonsillectomy.

Thrombocytes (platelets) are the smallest cellular elements of blood. They play a role in stopping bleeding. Sticking together, they form a plug in bleeding regions. Normally, 1 mm<sup>3</sup> of blood contains 150,000-400,000 thrombocytes. Likewise, TLO has been calculated in many studies and similar results to that of NLO were obtained. Although there are numerous studies on TLO, there is not much concerning ENT practice. Chen et al. reported TLO to be an independent predictor of disease-free survival after resection in oral squamous cell carcinoma [8]. Acharya et al. demonstrated that TLO is superior to NLO in indicating lymph node metastasis in oral cavity cancer [9]. Öztürk et al. used TLO in predicting local recurrence in the period of disease-free survival in early-stage tongue cancer [10]. There are studies suggesting that TLO also can be used as a prognostic biomarker in COPD [11], pulmonary embolus [12], diabetic ketoacidosis [13], and colorectal cancer [14] in addition to ENT. However, we found no study within the ENT discipline. In the present study, we determined no difference between the groups in terms of mean thrombocyte count. In other words, thrombocyte count was similar in both groups. However, we determined significant difference between TLO values. TLO was significantly higher in the study group as compared to the control group, suggesting that elevated TLO is not the consequence of high thrombocyte count but low lymphocyte count, which is the denominator.

We determined no difference between the tonsillectomy group and the control group in terms of RDW, which suggests that tonsillitis has no impact on erythrocytes.

### Conclusion

In conclusion, we determined a higher NLO in the patients who underwent tonsillectomy as compared to the control group. While elevated NLO in oncological patients is due to increased neutrophil count, in the present study of tonsillectomy patients we observed that elevated NLO is due to decreased lymphocyte count. We also determined that the value of TLO is higher in the patients who underwent tonsillectomy as compared to the control group, due to the fact that lymphocyte count decreased while thrombocyte count did not increase. We think that the NLO value  $\geq 1.48$ , which we observed prior to the tonsillectomy procedure, cannot be considered a definitive indication for tonsillectomy, but it is a parameter that can strengthen already-established indications.

Further large-series studies may be able to identify absolute NLO values as standards for certain pathologies. This is the only way to compare different samples properly.

### Competing interests

The authors declare that they have no competing interests.

### References

1. Kilickaya MM, Tuz M, Yariktas M, Yasan H, Aynali G, Bagci O. The Importance of the Neutrophil-Lymphocyte Ratio in Patients with Idiopathic Peripheral Facial Palsy. *Int J Otolaryngol* 2015; DOI:10.1155/2015/981950.
2. Atan D, Ozcan KM, Koseoglu S, Ikinogullari A, Cetin MA, Ensari S, et al. New predictive parameters of nasal polyposis: neutrophil to lymphocyte ratio and platelet to lymphocyte ratio *Kulak Burun Bogaz Ihtis Derg.* 2015;25(2):97-101.
3. Kilickaya MM, Aynali G, Tuz M, Bagci O. Is There A Systemic Inflammatory Effect of Cholesteatoma? *Int Arch Otorhinolaryngol* 2016; DOI: 10.1055/s-0036.
4. Senturk M, Azgin I, Ovet G, Alatas N, Agirgol B, Yilmaz E. The role of the mean platelet volume and neutrophil-to-lymphocyte ratio in peritonsillar abscesses. *Braz J Otorhinolaryngol* 2016; 82(6):662-7.
5. Ulu S, Ulu MS, Bucak A, Ahsen A, Yucedag F, Aycicek A. Neutrophil-to-lymphocyte ratio as a new, quick, and reliable indicator for predicting diagnosis and prognosis of idiopathic sudden sensorineural hearing loss. *Otol Neurotol* 2013;34(8):1400-4.
6. Derin S, Erdogan S, Sahan M, Topal H, Sozen H. Neutrophil-Lymphocyte Ratio in Patients with Adenoidectomy. *J Clin Diagn Res* 2016;10(3):3-5
7. Yenigun A. The efficacy of tonsillectomy in chronic tonsillitis patients as demonstrated by the neutrophil-to-lymphocyte ratio. *J Laryngol Otol* 2015;129(04):386-91.
8. Chen S, Guo J, Feng C, Ke Z, Chen L, Pan Y. The preoperative platelet-lymphocyte ratio versus neutrophil-lymphocyte ratio: which is better as a prognostic factor in oral squamous cell carcinoma? *Ther Adv Med Oncol* 2016;8(3):160-7.
9. Acharya S, Rai P, Hallikeri K, Anehsur V, Kale J. Preoperative platelet lymphocyte ratio is superior to neutrophil lymphocyte ratio to be used as predictive marker for lymph node metastasis in oral squamous cell carcinoma. *J Investig Clin Dent* 2016; DOI: 10.1111/jicd.12219.
10. Ozturk K, Akyildiz NS, Uslu M, Gode S, Uluoz U. The effect of preoperative neutrophil, platelet and lymphocyte counts on local recurrence and survival in early-stage tongue cancer. *Eur Arch Otorhinolaryngol* 2016;273(12):4425-9.
11. Karadeniz G, Aktogu S, Erer OF, Kir SB, Doruk S, Demir M, et al. Predictive value of platelet-to-lymphocyte ratio in exacerbation of chronic obstructive pulmonary disease. *Biomark Med* 2016;10(7):701-10.
12. Karatas MB, Ipek G, Onuk T, Gungor B, Durmus G, Canga Y, et al. Assessment of Prognostic Value of Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte Ratio in Patients with Pulmonary Embolism. *Acta Cardiol Sin* 2016;32(3):313-20.
13. Liu W-Y, Lin S-G, Wang L-R, Fang C-C, Lin Y-Q, Braddock M, et al. Platelet-to-Lymphocyte Ratio: A Novel Prognostic Factor for Prediction of 90-day Outcomes in Critically Ill Patients With Diabetic Ketoacidosis. *Medicine* 2016;95(4):1-7.
14. You J, Zhu G-Q, Xie L, Liu W-Y, Shi L, Wang O-C, et al. Preoperative platelet to lymphocyte ratio is a valuable prognostic biomarker in patients with colorectal cancer. *Oncotarget* 2016;7 (18):1-12.

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